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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/941,947	08/29/2001	Patricia C. Brzostowicz	CL1903 US NA	6363
23906	7590	07/01/2004	EXAMINER	
E I DU PONT DE NEMOURS AND COMPANY LEGAL PATENT RECORDS CENTER BARLEY MILL PLAZA 25/1128 4417 LANCASTER PIKE WILMINGTON, DE 19805			NASHED, NASHAAT T	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/941,947

Applicant(s)

BRZOSTOWICZ ET AL.

Examiner

Nashaat T. Nashed, Ph. D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 August 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6-8, 10, 12, 13, 15, 17, 19, 21, 23, 25, 27, 35, 37-40 and 48-50 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-8, 10, 12, 13, 15, 17, 19, 21, 23, 25, 27, 35, 37-40, and 48-50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 12/17/01, 9/27/02, 1/27/03
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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The application has been amended as requested in the communication filed January 7, 2004. Accordingly, claims 5, 9, 11, 14, 16, 18, 20, 22, 24, 26, 28-34, 36, and 41-47 have been canceled, and claims 8, 39, and 48 have been amended.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. 112, first paragraph, as the specification lacks a sufficient written description for enablement based on deposit requirement.

The invention appears to employ a novel microorganism. Since the microorganism is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The enablement requirement of 35 U.S.C. 112 may be satisfied by deposit of the microorganism. The specification does not disclose a repeatable process to obtain the microorganism and it is not apparent if the microorganism is readily available to the public. Accordingly, it is deemed that a deposit of the microorganism should have been made in accordance with 37 C.F.R. 1.801-1.809.

It is noted that the applicant has deposited the *methylobionas 16a*, page 9, lines 15-19, but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by the applicant, or a statement by an attorney of record over his/her signature and registration number, stating that the specific microorganism has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809, the applicant may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his/her signature and registration number, showing that:

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- (1) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
- (2) all restriction upon availability to the public will be irrevocably removed upon granting of the patent;
- (3) the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and
- (4) the deposit will be replaced if it should ever become inviable.

Claims 12, and 38 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 1-4, 6, 7, 10, 13, 15, 17, 19, 21, 23, 25, 27, 35, 39, 40, and 48-50 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to a method of making carotenoids utilizing a transformed methylomonase with genes required for the biosynthesis of carotenoids. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to all possible organisms, which are able to metabolize C1 compounds such as methane, methanol, formaldehydes, formic acid, methylated amines, and methylated thiols. Factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses a method utilizing any transformed organism with at least one nucleic acid encoding an enzyme on the biosynthetic pathway of any carotenoid, said organism is capable to metabolize-/assimilate any single carbon compound. The specification provides guidance and examples in the form of an assay to isolate and sequence the genome of methylomonase 16a (example 1), identified the expression of the genes encoding both Embden-Myerhof, and Entner-Doudoroff carbon pathways in the wild-type (examples 4 and 5), transform said methylomonase with nucleic acid encoding the genes required for the biosynthesis of carotenoids, and producing carotenoids on an industrial scale using the transformed methylomonase grown only on methane. While molecular biological techniques and genetic manipulation to make and use the constructs claimed are known in the prior art and the skill of the artisan are well developed, knowledge regarding all possible organisms capable of growing on efficiently on C1 compound, where to find them, their gene sequence, and molecular biology is lacking. The specification teaches special characteristics of methylomonas 16a, which makes it uniquely suitable for the claimed method. Thus, searching for a suitable organism,

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which metabolized C1 compounds having similar characteristics to methylomonas 16a is well outside the realm of routine experimentation and predictability in the art of success is extremely low. The amount of experimentation to identify a suitable organism is enormous. Since routine experimentation in the art does not include screening vast numbers of organisms isolated from various locations where the expectation of obtaining the desired organism is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the various organisms which are suitable for making carotenoides and growing on C1 compounds such as methane, methanol, formaldehyde, formic acid, methylated amins, and methylated thiols. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-4, 6-8, 10, 12, 13, 15, 17, 19, 21, 23, 25, 27, 35, 37, 38-40, and 48-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

- (a) The phrase "suitable levels of isopentenyl pyrophosphate" in claims 1, 39, and 49 render the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Neither the claim or the specification define the suitable levels of isopentenyl pyrophosphate that is required to carry out the claimed method; and one of ordinary skill in the art would not know said suitable levels.
- (b) The phrase "C1 carbon substrate methylated amines, methylated thiols" in claim 2 render the claims indefinite and confusing because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. The definition stated in the specification for C1 carbon substrate on page 11, lines 4-7, is repugnant to one of ordinary skill in the art. A C1 substrate is a chemical compound comprising a single carbon atom such as methan, methanol, methylamine or methylmercatane. Dimethyl and trimethylamine are C2 and C3 compounds, respectively. Also, dimethylmercaptan is a C2 compound.
- (c) Claim 38 recites the limitation "wherein said methanotropic bacteria" in claim 1. There is insufficient antecedent basis for this limitation in the claim.
- (d) Claim 3, 4, 6-8, 10, 12, 13, 15, 17, 19, 21, 23, 25, 27, 35, 37, 40, 48, and 50 are included in this rejection because they are dependent on rejected

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claims and do not correct the deficiencies of the claim from which they depend.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 13, and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by U. S. patent 5,545,816 [Ausich *et al.* ('816), see IDS].

The '816 patent teaches the transformation of plants cells with nucleic acid sequences encoding geranylgeranyl pyrophosphate (GGPP) synthase and phytone synthase and a method of producing phytoene from the transgenic plant, see lines 29-67 of column 22. Example 9 teaches the production of lutein in tobacco plant. Since each plant cell contain chloroplast and capable of metabolizing/assimilating carbon dioxide (a C1 substrate), the method described in example 9 of the '816 patent is considered identical to the claimed method of claims 1, 2, and 48.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 39, 40, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over '816 patent in view Albrecht *et al.* [see IDS: Biotech. Lett. (1991) 21, 791-795].

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The teaching of '816 patent are summarized above.

Albrecht *et al.* teach that the transformation of *E. coli* producing β -carotene with nucleic acid encoding required in the biosynthesis of prenyl pyrophosphates lead to an increase in the production of β -carotene, see the abstract. Specifically, they teach the transformation of an *E. coli* harboring a carotenoid gene cluster with the genes *dxs* for over expression of 1-deoxy-D-xylulose 5-phosphate, *dxr* for 1-deoxy-D-xylulose 5-phosphate reductoisomerase, and *idi* encoding an isopentyl pyrophosphate isomerase. The modified *E. coli* producing β -carotene and zeaxanthin produced twice as much carotenoids compare to that without the *dxs* and *dxr* genes, see page 793, left column, second paragraph; and Table 2 on page 794.

Albrecht *et al.* provide one of ordinary skill in the art at the time of invention to introduce genes encoding enzymes required for the biosynthetic isopentyl pyrophosphate and dimethylallyl pyrophosphate as they teach transforming a host cell comprising carotenoid gene cluster with the *dxs*, *dxr*, and *idi* genes lead to increase in the production of carotenoids by said cell. It would have been obvious to one of ordinary skill in the art to further transform the host plant cell containing the carotenoid gene cluster taught in '816 patent with at least the *dxs*, and *dxr* as taught by Albrecht *et al.* to increase the amount of carotenoid produced by the plant cell (claims 39, 40, and 49). Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, clearly *prima facie* obvious.

Claims directed a method of making carotenoids utilizing a transformed methyl-omonase and free of rejection(s) under 35 U.S.C. 112, second paragraph, would be considered favorably.

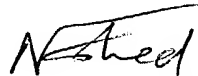
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Nashaat T. Nashed, Ph. D.
Primary Examiner
Art Unit 1652